VANCOMYCIN RESISTANCE IN ENTEROCOCCI

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Glycopeptide antibiotics such as vancomycin act by binding to the D-alanyl-D-alanine terminus of stem pentapeptides present in bacterial peptidoglycan. The D-alanyl-D-alanine terminus is recognized by a number of enzymes required for cell wall synthesis, and was believed to be ubiquitous among eubacterial peptidoglycan. Thus the emergence of vancomycin resistance, in the absence of a simple barrier to vancomycin binding such as the outer membrane of gram-negative bacteria, was considered highly unlikely. Nonetheless, glycopeptide resistance has recently been recognized among several gram-positive species. Since the first identification of highly vancomycin-resistant enterococci in 1988, these organisms have become prevalent throughout the U.S. and Europe, and are now common nosocomial pathogens, particularly in intensive care units.

Plasmids isolated from highly vancomycin-resistant (VanA phenotype) enterococci possess a cluster of genes associated with resistance, including the regulatory pair vanR-vanS, and at least 4 structural genes. Studies of sequence homology and analysis of cytoplasmic peptidoglycan precursors of resistant cells have shown that the structural genes vanH and vanA act together to produce a peptidoglycan precursor which terminates in the depsipeptide D-alanyl-D-lactate rather than D-alanyl-D-alanine. Stem peptides terminating in the depsipeptide are not bound by vancomycin, allowing peptidoglycan synthesis to occur in the presence of the antibiotic. Also present in the van gene cluster are vanX, of unknown function, and vanY, encoding a D,D-carboxypeptidase which acts on both cytoplasmic pentapeptide precursors and the dipeptide D-alanyl-D-alanine, and which may enhance survival in the presence of vancomycin.

Source: https://www.industrydocuments.ucsf.edu/docs/fgmv0000